REMARKS

Claims 1-4, and 7-12 are pending (previously restricted to SEQ ID NOS:34-38), claims 5 and 6 having been cancelled without prejudice, the limitations thereof having been recited in *independent* claim 1 (Previously amended).

Applicants thank the Examiner for considering the Affidavit of Dr. Cathy Lofton-Day in support of the inventive diagnostic utility, and for the Examiner's comments thereon. Applicants also thank the Examiner for withdrawal of particular rejections.

Applicants acknowledge the Examiner's *new* 35 U.S.C. § 112 ¶ 1 rejection, based on alleged 'new matter.'

Applicants acknowledge the Examiner's *maintained* rejections under 35 U.S.C. § 112 ¶ 1, based on alleged lack of written description and enablement.

Applicants acknowledge the Examiner's new grounds of rejection under 35 U.S.C. § 102 (b), in view of Nelson et al. (US 5,552,277).

Applicants have responsively amended the pending claims to remove the alleged new matter and bring the scope of the claims into conformity with the specification in view of the Examiner's comments.

Applicants respectfully request reconsideration of the above-identified patent application in view of the current amendments and following remarks. No new matter has been added.

Rejections under 35 U.S.C. § 112, ¶1

Written Description and New Matter Rejections

The Examiner rejected claims 1-2 and 4 under 35 U.S.C. § 112, ¶1, "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention" (Office action of 08 August 2003, at page 2, para 4).

Specifically, the Examiner asserts that the claims as written, do not require that the CpG is contiguous, but rather only requires that the sequence contain a single nucleotide of SEQ ID NO:35-38.

Applicants respectfully maintain the reassert applicant rebuttal arguments of record. Applicants have, nonetheless, further amended independent claims 1 to recite "and coordinately methylated contiguous CpG island sequences that comprise a DNA sequence selected from the

group consisting of SEQ ID NOS:34-38, wherein a CpG island sequence is a contiguous sequence of about 0.2 to about 1 kb in length that satisfies the criteria of having both a frequency of CpG dinucleotides corresponding to an Observed/Expected Ratio >0.6, and a GC Content >0.5.

Thus, applicants, in response to the Examiner's comments, have clarified that the CpG island must be *contiguous*, and have additionally required that the CpG island *comprise* either SEQ ID NO 36 or 37, and have yet further required that the CpG island be *coordinately regulated* with the comprised sequence. The combination of the requirement SEQ ID NO 36 or 37 be comprised within such a CpG island, along with the explicit definition of a CpG island and a requirement for coordinate methylation provides more than enough written description to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, and unambiguously identify the subject CpG islands.

Support in the specification for CpG islands being associated with SEQ ID NOS:36 or 37 is found in the "Description" column of Table 2 at page 9 of the Specification. The level of skill in the art to sequence DNA and determine coordinate regulation is high.

The Examiner also rejected claims 1, 2, 4 and 7-12 under 35 U.S.C. § 112, ¶1, lacking sufficient written description (*Id*, at page 3, para 5).

Applicants contend that the above-described amendments requiring that the CpG islands *comprise* either SEQ ID NO:36 or 37, in fact provides enough clarity under both the Vas-Cath and Eli Lilly standards cited by the Examiner. Indeed, the furthermore requirement for the presence of either SEQ ID NO:36 or 37 with the claimed CpG island sequences provides suitably precise definition in terms of "structure, formula, chemical name, or physical properties."

Claim 2 has been amended to conform to independent claim 1.

Applicants, therefore, respectfully request withdrawal of the Examiner's new matter rejection with respect to pending amended claims 1, 2 and 4.

Enablement

The Examiner rejected claims 1-2, 4 and 7-12 under 35 U.S.C. § 112, ¶1, based on lack of enablement (*Id*, at page 8)

Specifically, the Examiner alleges that the Specification fails to adequately describe

contiguous CpG island regions of SEQ ID NOS:35-38.

Applicants have addressed this argument herein above, and thus will not repeat it here.

Additionally, the Examiner continues to misconstrue in a *mantra*-like fashion, applicants' own statements in the specification, alleging that they undermine and contradict the claimed utility (*Id*, citing, *inter alia*, the instant specification at page 2 lines 31-35). Applicants respectfully view the Examiner's continuing position on the alleged meaning of these statements as a form of tortured harassment, and opt to stand by applicants' explanation and rebuttals of record.

The Examiner further misconstrues applicants disclosure by asserting (page 11, line 4 of the present Office Action) that "the bladder cancer samples exemplified in the specification do not appear to have hypermethylation of SEQ ID NO:34-38." In fact, the bladder cancer samples exemplified in the specification are all characterized by hypermethylation of SEQ ID NO:34-38, as is evident from Table 2 on pages 8-10, where sequences are sub-grouped into either *hyper*-(top half of the Table continuing to mid page 9) or *hypo*-methylation (bottom half of the Table starting from page 9 and going to page 10).

The Examiner further alleges that the affidavit of Dr. Cathy Lofton-Day (of record) supports diagnostic utility only for SEQ ID NOS:36 and 37, and only then in particular cancers (page 13-14 of the present Office Action)

To facilitate prosecution, applicants have amended independent claim 1 to recite only SEQ ID NOS:36 and 37 in the context of breast and colon cancer.

Additionally, applicants have added new claims 13-16, which recite only SEQ ID NO:37 in the context of breast, colon and prostate cancer.

Rejections under 35 U.S.C. § 102

The Examiner has asserted yet another new grounds of rejection of claim 1 under 35 U.S.C. § 102 as being anticipated by Nelson et al. (US Pat. 5,552,277, September 1996) (Office Action of 08 August 2003, at page 16).

The Examiner asserts that under the present claim language, the GSTP1 promoter sequence of Nelson anticipates the present invention because the GSTP1 sequence of Nelson contains a C or a G.

Applicants point out that applicants' language requires more that a mere presence of a C or a G in a CpG island, but rather the present of an overlapping C or G between the island and the

coordinately regulated sequence. The Examiner's position is thus not well taken.

Regardless, as discussed in detail above, applicants have amended claim 1 (and as reflected in conforming new claim 13) to require that the subject CpG islands comprise either SEQ ID NO:36 or 37. Nelson does not anticipate the former claim language, and certainly not the presently amended independent claims 1 and 13.

Applicants, therefore, respectfully request withdrawal of the Examiner's 35 U.S.C. § 102 anticipation rejection under Nelson et al. with respect to claim 1

Conclusion

In view of the foregoing amendments and remarks, applicants respectfully request reconsideration of the claimed invention, entry of the present responsive Amendment and allowance of all pending claims 1 (Currently amended), 2 (Currently amended), 4 (Previously amended), 7 (Previously amended), 8 (Previously amended), 9 (Currently amended), 10 (Currently amended), 11 (Original), 12 (Original) and 13-16 (New).

Respectfully submitted,

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